REMARKS

Objection to the Specification and Rejection of Claims 1, 2, 4, 6, 7, 14-31, 33, 39, 40, 53 and 54 Under 35 U.S.C. § 112, First Paragraph:

The Examiner has objected to the specification and rejected Claims 1, 2, 4, 6, 7, 14-31, 33, 39, 40, 53 and 54 under 35 U.S.C. § 112, first paragraph, contending that the specification is insufficient to enable one of skill in the art to practice the claimed invention without undue experimentation. Initially, the Examiner acknowledges that Applicant's prior amendments and arguments have addressed the previously presented portion of this rejection with regard to whether or not certain diseases are Th1 or Th2 mediated and the oversimplicity of the Th1/Th2 paradigm. However, the Examiner contends that two issues remain. First, the Examiner contends that with regard to Burnet et al., which was previously cited by the Examiner to support the position that "attempts to skew the Th1/Th2 ratio might be dangerous", the Examiner quotes Wohlleben et al. and concludes that in 2002, at least Burnet et al. and Wohlleben et al. were not of the opinion that the induction of a Th1[sic] response *in vivo* was acceptable treatment for allergy. The Examiner states that "[w]hile the idea might have potential, the idea did not rise to the level of invention". Second, the Examiner contends that in all experiments disclosed in the specification, the heat shock protein was administered before the induction of disease "i.e., airway hyperresponsiveness or eosinophilia". Thus, the Examiner concludes that there is no evidence of record that the claimed method could be used to reduce an ongoing inflammatory response.

Applicants traverse the rejection of Claims 1, 2, 4, 6, 7, 14-31, 33, 39, 40, 53 and 54 under 35 U.S.C. § 112, first paragraph. First, with regard to the issue of Burnet et al., the only stated or implied basis for the Examiner's enablement rejection in view of Burnet et al. (with further reference to Wohlleben et al.) is based on the allegation that such a therapy might be dangerous because it could lead to Th1-mediated pathology, rather than cure the allergy. The Examiner appears to have otherwise acknowledged that the present invention, as claimed, is enabled, with the exception of the second item pertaining to timing of administration, which is discussed below. Therefore, the Examiner's rejection on this point relates to an alleged issue of safety to the patient. However, Applicants submit that both the Patent Office and the courts have long held that the Patent Office

should confine its review of patent applications to the statutory requirements of the patent laws, and that the issue of safety is not a sufficient reason to reject a claim on the basis of enablement. As set forth in MPEP 2164.01(c), with regard to the issue enablement and specifically, issues regarding how to use the claimed invention:

"The Applicant need not demonstrate that the invention is completely safe".

Furthermore, as stated in MPEP 2107.03(V):

> "[o]ther agencies of the government have been assigned the responsibility of ensuring conformance to standards established for the advertisement, use, sale or distribution of drugs. The FDA provides a two-prong test to provide approval for testing. Under that test, a sponsor must show that the investigation does not pose an unreasonable and significant risk of illness or injury"; and
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> "it is improper for Office personnel to request evidence of safety in the treatment of humans, or regarding the degree of effectiveness. See *In re* Sichert, 566 F.2d 1154, 196 USPQ 209 (CCPA 1977); *In re Hartop*, 311 F.2d 249, 135 USPQ 419 (CCPA 1962); *In re Anthony*, 414 F.2d 1383, 162 USPQ 594 (CCPA 1969); *In re Watson*, 517 F.2d 465, 186 USPQ 11 (CCPA 1975); *In re Krimmel*, 292 F.2d 948, 130 USPQ 215 (CCPA 1961); *Ex parte Jovanovics*, 211 USPQ 907 (Bd. Pat. App. & Inter. 1981)".

The Examiner apparently accepts that the present invention has an asserted utility that is credible and accordingly, there is no basis in the statutory requirements for utility or enablement that Applicants demonstrate that the claimed method is completely safe for humans. Indeed, many therapeutic treatment regimens have *serious* side effects, and yet are used clinically because they also provide a substantial benefit to the patient. It is not the place of the Patent Office to require Phase II testing of the claimed method in order to prove utility or enablement of an invention. As previously discussed, a concern over whether the method of the present invention *might* have undesirable side effects or *might* contribute to the development of a different disease, which are only *suggestions* by Burnet et al. based on suggested correlations, does not negate the utility, value or ability of the present invention to provide a benefit to the patient suffering from a hypereosinophilic or

inflammatory condition associated with AHR. With regard to the Examiner's statement that "[w]hile the idea might have potential, the idea did not rise to the level of invention", it is Applicants' position that this statement is misplaced. The ideas of Burnet et al. and Wohlleben et al. are not the invention under review and do not rebut the demonstration by the present inventor of the presently claimed invention.

Finally, Applicants submit that at the time of the invention, studies had already shown that administration of HSP-65 to humans was well tolerated. In support of this position, enclosed is a press release from StressGen Biotechnologies Corp. of May 22, 2000, which shows that human patients receiving a recombinant fusion protein comprising HSP-65 for the treatment of patients with human papillomavirus infection tolerated the protein, with only mild adverse side effects.

Second, with regard to the issue of when the heat shock protein is administered, Applicants initially note that the HSP was administered to the animals *after* allergic sensitization, but before the actual induction of an acute airway response (constriction), for example, using methacholine (a stimulus). Therefore, the HSP was not administered before induction of the disease, but rather before induction of an acute response in an animal that was already sensitized to the allergen. Airway inflammation and airway hyperresponsiveness (AHR) are not single episodes in a patient with an allergic inflammatory disease, but rather, these are ongoing conditions that are associated with the disease. With regard to AHR, the specification teaches that AHR is an abnormality of the airways that allows them to narrow too easily and/or too much in response to a stimulus capable of inducing airflow limitation (*e.g.*, see page 27, lines 2-6). Therefore, a patient can have ongoing or chronic AHR but not presently be experiencing an acute episode of airway hyperresponsiveness, or bronchoconstriction or airflow limitation, as occurs in response to a stimulus. Applicants note that only a "reliever", such as a bronchodilator, can reverse the immediate constriction in an acute attack of airway constriction in a patient that has AHR. The treatment of the present invention represents a second type of control over AHR, which can be referred to as a "controller". A controller acts to reduce the occurrence, severity or frequency of the episodes of acute bronchoconstriction in a patient, thus reducing or preventing AHR in the patient. As a result of administration of the controller, when bronchoconstriction is induced by a stimulus, the airway responsiveness to the stimulus is reduced

toward a normal response (*i.e.*, the response to the stimulus that would occur in an individual who does not suffer from AHR). Therefore, such a treatment can be administered at any time to a patient that has AHR, including before or after a given episode of actual bronchoconstriction. Similarly, in a patient with allergic inflammation, airway eosinophilia will increase upon exposure to allergen challenges or stimuli. Again, the method of the present invention controls the eosinophilia, so that the occurrence, severity or frequency of the episodes of eosinophilic infiltration into the airways of the patient is decreased. Therefore, as with AHR, the treatment can be administered at any time to a patient that has eosinophilia, including before or after a given episode of actual eosinophilic airway infiltration. Accordingly, Applicants submit that the claims are commensurate in scope with what is described in the specification.

In view of the foregoing discussion, Applicants respectfully request that the Examiner withdraw the rejection of Claims 1, 2, 4, 6, 7, 14-31, 33, 39, 40, 53 and 54 under 35 U.S.C. § 112, first paragraph.

Applicants have attempted to respond to all of the concerns set forth in the August 1, 2005 Office Action, and submit that the claims are in a condition for allowance. In the event that the Examiner has any further concerns regarding Applicants' position, he is encouraged to contact the below-named agent to expedite prosecution.

Respectfully submitted,

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